

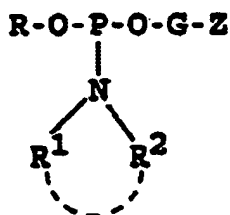


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| (21) International Application Number: PCT/US92/05897<br>(22) International Filing Date: 14 July 1992 (14.07.92)<br>(30) Priority data:<br>731,055 15 July 1991 (15.07.91) US<br>(71) Applicant: LA JOLLA PHARMACEUTICAL COMPANY [US/US]; 6455 Nancy Ridge Drive, Suite 300, San Diego, CA 92121 (US).<br>(72) Inventors: JONES, David, S. ; 11265 Florindo Road, San Diego, CA 92127 (US). HACHMANN, John, P. ; 12275 Carmel Vista Road, #128, San Diego, CA 92130 (US). CONRAD, Michael, J. ; 11336 Penanova Street, San Diego, CA 92129 (US). COUTTS, Stephen ; 6151 Rancho Diegueno Road, Rancho Santa Fe, CA 92067 (US). LIVINGTON, Douglas, Alan ; 5260 Fiore Terrace, #115, San Diego, CA 92122 (US). |  | (74) Agents: CIOTTI, Thomas, E. et al.; Morrison & Foerster, 755 Page Mill Road, Palo Alto, CA 94304 (US).<br>(81) Designated States: BB, BG, BR, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG).<br><br>Published<br>With international search report. |   |

(54) Title: MODIFIED PHOSPHOROUS INTERMEDIATES FOR PROVIDING FUNCTIONAL GROUPS ON THE 5' END OF OLIGONUCLEOTIDES



(II)

## (57) Abstract

Phosphoramidites of formula (II) where R is a base-labile protecting group, R<sup>1</sup> and R<sup>2</sup> are individually alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 8 carbon atoms, aryl of 6 to 20 carbon atoms or are joined together to form with the nitrogen atom a cyclic structure of 4-7 carbon atoms and 0 to 1 annular chalcogen atoms of atomic number 8 to 16, G is a hydrocarbylene group of 1 to 20 carbon atoms and Z is a hydroxy-protected vicinal diol group bound to G by one of the vicinal diol carbon atoms of a disulfide group and bound to G by one of the sulfur atoms of the disulfide group, with the proviso that G is of at least 4 carbon atoms when Z is said disulfide group are used in conventional automated oligonucleotide synthesis to introduce a functional aldehyde or thiol group on the 5' end of the oligonucleotide to thereby provide a reactive site on the oligonucleotide that may be used to conjugate the oligonucleotide to molecules that contain a free amino group or an electrophilic center reactive with a thiol group.